

HPV ROBUST SUMMARIES
FOR
TRIXYLENYL PHOSPHATE

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CAS No. 25155-23-1

June 16, 2004

Submitted By:

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Trixylenyl Phosphate – Robust Summaries

1. Substance Information

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|-----------------------------|---|
| CAS Number: | 25155-23-1 |
| Chemical Name: | Trixylenyl phosphate |
| Physical State: | Liquid |
| Purity: | 100% |
| Impurity: | None |
| Synonyms: | Phenol dimethyl phosphate TXP Phosphoric acid, trixylyl ester Trixylyl phosphate Xylenol, phosphate ester |
| Product Description: | Commercial trixylenyl phosphate is not a single chemical entity. It consists of over 50 different components, many of which are structural isomers. |
| Commercial Products: | Phosflex TXP, Kronitex TXP, Fyrquel EHC, Fyrquel EHC-N |
| Uses: | Used as a lubricant additive, a plasticizer in plastics, and as a component of hydraulic fluids |
| Exposure Limits: | None |

2. Physical – Chemical Properties

2.1 Boiling Point:

| | |
|--------------|--|
| Identity: | Trixylenyl phosphate |
| Method: | Not stated |
| Year: | Not known |
| GLP: | Not known |
| Value: | 243-265°C at 10 mm Hg |
| Conclusion: | The boiling point of trixylenyl phosphate is 243-265°C |
| Reliability: | 4 |
| Reference: | 1 |

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2.2 Vapor Pressure:

Identity: Trixylenyl phosphate
Method: Not stated
Year: Not known
GLP: Not known
Value: 0.133 hPa at 37.8°C
Conclusion: The vapor pressure of trixylenyl phosphate is 0.133 hPa at 37.8°C
Reliability: 2
Reference: 2

2.3 Density/Specific Gravity

Identity: Trixylenyl Phosphate
Method: Not stated
Year: Not known
GLP: Not known
Value: 1.16 @ 25°C
Conclusion: The density of trixylenyl phosphate is 1.16 @ 25°C.
Reliability: 4
Reference: 1

2.4 Water Solubility

Identity: Phosflex TXP (Lot No. 02223D0200)
Guideline: OPPTS 830.7860 and OECD 105
Method: Generator Column Method
Year: 2003
GLP: Yes
Value: 18.6 ug/l @ 25°C
Conclusion: The water solubility of trixylenyl phosphate is 18.6 ug/l @ 25°C
Reliability: 1
Reference: 3

2.5 Octanol:Water Partition Coefficient

Identity: Trixylenyl Phosphate
Method: Not stated
Year: 1979
GLP: No
Value: Log Kow = 5.63 @ 25°C
Conclusion: The n-octanol:water partition coefficient (log Kow) of trixylenyl

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phosphate was determined to be 5.63 @ 25°C.
Reliability: 2
Reference: 4

3. Environmental Fate

3.1 Photodegradation

Identity: Phosflex TXP (Lot No. 02223D0200)
Guideline: OPPTS 830.7050 and OECD 101
Year: 2003
GLP: Yes
Method: The test determined the ultraviolet-visible absorption spectrum of the test substance under acidic, neutral, and basic conditions using spectrophotometric methods. The determinations were made at 25°C. Test substance solutions were prepared in hydrochloric acid, reagent water/methanol, and sodium hydroxide to provide samples at pH of < 2, ~ 7, and > 10, respectively. Methanol blanks were included in the analyses. Spectra were measured over the wavelength range of 190 to 800 nanometers.
Results: The mean molar absorption coefficients obtained at each of the three pH are 1455, 1368, and 1809 l/mol-cm for pH < 2.7, 7, and > 10, respectively. Under conditions of acidic and neutral pH, the bandwidths were 21.6 and 21.9 nm, respectively. The test substance was not stable under basic conditions and a bandwidth could not be established.
Conclusion: The mean molar absorption coefficients at pH < 2.7, 7, and > 10 were determined to be 1455, 1368, and 1809 l/mol-cm, respectively.
Reliability: 1
Reference: 5

3.2 Stability in Water

Identity: Phosflex TXP (Lot No. 02223D0200)
Guideline: OPPTS 835.2110 and OECD 111
Year: 2003
GLP: Yes
Method: A preliminary hydrolysis study was conducted in which the test substance was maintained in buffered water at pH 4, 7, and 9, at 50°C, for five days. Day 0 and day 5 waters were analyzed by LC/MS to determine the total amount of test substance present. Calibration curves were included both days to assure accurate quantitation. The pH 4 buffer consisted of sodium acetate adjusted with acetic acid, the pH 7 buffer was potassium

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| | <p>dihydrogen phosphate, and the pH 9 buffer contained boric acid and potassium chloride. Because significant hydrolysis was observed in five days at 50°C in the preliminary study at pH 7 and 9, a definitive hydrolysis test was conducted over a longer period, at 15°C and at 25°C, using the same buffer systems. LC/MS was again used in the definitive study to determine hydrolysis of the test substance. The test substance was measured at 10 sampling intervals during the test.</p> |
| Results: | <p>In the preliminary test, the test substance hydrolyzed 24.6% and 34.3% in 5 days at 50°C at pH 7 and 9, respectively. Hydrolysis at pH 4 was not significant. The hydrolytic half-life under acidic conditions is estimated to be greater than one year. In the definitive study, at pH 7, hydrolysis was not observed over a 28 day period at temperatures of 15°C and 25°C. Thus the half-life of trixylenyl phosphate at pH 7 is estimated to be greater than one year. At pH 9, marginal hydrolysis occurred at 25°C which provided an estimated half-life of 219 days. There was no significant hydrolysis at pH 9 at 15°C over 33 days.</p> |
| Conclusion: | <p>Trixylenyl phosphate is hydrolytically stable at pH 4 and 7, providing half-lives of greater than one year. Slight hydrolytic degradation occurs at pH 9. Regression analyses performed on the data obtained at 25°C show the half-life of trixylenyl phosphate under alkaline conditions to be about 219 days.</p> |
| Reliability: | 1 |
| Reference: | 6 |

3.3 Biodegradation

| | |
|------------|---|
| Identity: | Phosflex TXP (Lot No. 02223D0200) |
| Guideline: | OPPTS 835.3110 and OECD 301D Closed Bottle Test |
| Year: | 2003 |
| GLP: | Yes |
| Method: | <p>A growth medium inoculated with a wastewater treatment facility microbial culture ("inoculum"), and was subsequently dosed with trixylenyl phosphate, which was the sole source of organic carbon for the microbes. Biodegradation of the test substance was followed over a 28-day test period by analyzing the amount of dissolved oxygen present. Sodium benzoate, a chemical known to readily biodegrade, was added to another chamber as a positive control. The amount of dissolved oxygen used in the test system is expressed as a percentage of the theoretical oxygen demand (ThOD) or chemical oxygen demand (COD) of the test substance. Each group contained ten replicate containers. Measurements of dissolved oxygen were taken on test days 0, 7, 14, 21, and 28.</p> |
| Results: | <p>The average percentage biodegradation of trixylenyl phosphate on days 7, 14, 21, and 28, as determined by measurement of dissolved oxygen, was essentially zero. The reference substance, sodium benzoate, degraded within the acceptable range, indicating that the inoculum was active.</p> |

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Since trixylenyl phosphate did not achieve a 60 percent ThOD or COD, the criteria for ready bioavailability, it is classified as not readily biodegradable.

Conclusion: Trixylenyl phosphate is not readily biodegradable.
Reliability: 1
Reference: 7

4. Ecotoxicity

4.1 Acute Toxicity to Fish

Identity: Phosflex TXP (Lot No. 02223D0200)
Guideline: OPPTS 850:1075 and OECD 203 96 Hr. Acute Toxicity Test in Fish
Year: 2003
GLP: Yes
Species: Fathead Minnow (*Pimephales promelas*)
Method: Groups of 20 fathead minnows were exposed to one of five nominal concentrations (125, 250, 500, 1000, and 2000 ug/l) of the test substance. Each test chamber contained 10 fish, and each dose concentration utilized two replicate test chambers. The water was analyzed to assure correct pH, dissolved oxygen, hardness, alkalinity, and other parameters. A non-treated control group and a solvent control group were included in the study. The solvent DMF was used to achieve water concentrations that exceeded the water solubility limit of the test substance. Mean measured water concentrations were determined from aliquots of water collected from each treatment and control chamber at the beginning of the test, at 48 hours, and at test termination (96 hours). The fish were exposed to trixylenyl phosphate for 96 hours using a flow-through system. The LC50 and 95% confidence limits were calculated using the Spearman-Kärber method. The fish were observed daily for mortality, signs of toxicity, and abnormal behavior which, if seen, were recorded.

Results: The water analysis showed a pH of 8.3 to 8.4, total hardness of 132 mg/l as CaCO₃, total alkalinity of 186 mg/l as CaCO₃, and specific conductance of 325 umhos/cm. The water temperature was maintained at 22°C. The actual measured doses were 119, 227, 422, 787, and 1119 ug/l. There were no signs of toxicity in any group, and there was no mortality. The 96 hour LC50 was determined to be > 1119 ug/l. The 96 hour NOEC is 1119 ug/l, which is about 100 times the water solubility limit of trixylenyl phosphate.

Conclusion: The acute 96 hour LC50 was determined to be greater than 1119 ug/l, the highest dose administered in this test.

Reliability: 1
Reference: 8

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Identity: Fyrquel EHC (Lot No. 4795-13-6)
Guideline: Committee on Methods for Toxicity Tests with Aquatic Organisms
Year: 1979
GLP: No
Species: Rainbow trout (*Salmo gairdneri*)
Method: Groups consisting of 10 rainbow trout were exposed to one of five nominal concentrations (6.3, 12.5, 25, 50, and 100 mg/l) of the test substance. The water was analyzed to assure correct pH, dissolved oxygen, hardness, alkalinity, and other parameters. A non-treated control group was included in the study. Actual water concentrations of the test material were not measured. The fish were exposed to trixylenyl phosphate for 96 hours using a flow-through system. The fish in each group were observed every 24 hours for signs of toxicity and for mortality.
Results: The initial dissolved oxygen was 10.3 mg/l, the average temperature was 15.0°C, total hardness was 220 mg/l as CaCO₃, total alkalinity was 141 mg/l as CaCO₃, the pH was 7.47, and the specific conductance was 500 umhos/cm. There was no mortality in any group, and no signs of toxicity. The 96 hour LC50 for trixylenyl phosphate was determined to be greater than the nominal dose of 100 mg/l. This dose is more than 1000 times the water solubility limit of the test substance.
Conclusion: The acute 96 hour LC50 is greater than 100 mg/l.
Reliability: 2
Reference: 9

4.2 Acute Toxicity to Aquatic Invertebrates

Identity: Phosflex TXP (Lot No. 02223D0200)
Guideline: OPPTS 850.1010 and OECD 202 48 Hr. Acute Toxicity in Invertebrates
Year: 2003
GLP: Yes
Species: Cladoceran (*Daphnia magna*)
Method: Groups consisting of 20 daphnids were exposed to 8 concentrations of trixylenyl phosphate, namely nominal 16, 31, 63, 125, 250, 500, 1000, and 2000 ug/l, for 48 hours. The test was conducted under static-renewal conditions. The pH, dissolved oxygen concentration, water hardness and temperature were measured at 0, 24, and 48 hours. The actual water concentrations of trixylenyl phosphate to which the daphnid were exposed were determined by analytical measurement using HPLC. The solvent DMF was used to administer doses that exceeded the water solubility limit of the test substance. Negative control and solvent control groups were included in the study. The daphnid were observed at 4, 24, and 48 hours after test initiation for signs of toxicity, immobility, and death.
Results: The water temperature was maintained at 20°C, the dissolved oxygen at ≥7.8 mg/l (87% of saturation), and the pH ranged from 8.0 to 8.6. The

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water hardness and alkalinity were 124 mg/l and 186 mg/l as CaCO₃ respectively. The mean measured water concentrations at initiation, after renewal, and at termination were averaged, and the means were 11, 22, 49, 107, 232, 418, 903, and 1597 ug/l, representing 69, 71, 78, 86, 93, 84, 90 and 80% of the nominal concentrations, respectively. The NOEC was 11 ug/l. Percent mortality/immobility in the other groups at test termination ranged from 15% in the 22 ug/l group to 100% in the 107 ug/l and higher groups.

Conclusion: The 48 hour EC50 was determined to be 60 ug/l and the NOEC = 11 ug/l.
Reliability: 1
Reference: 10

4.3 Toxicity to Aquatic Plants

Identity: Phosflex TXP (Lot No. 02223D0200)
Guideline: OPPTS 850.5400 and OECD 201 96-Hour Alga Toxicity Test
Year: 2003
GLP: Yes
Species: *Selenastrum capricornutum* (freshwater alga)
Method: The phytotoxicity of the test substance was determined in the freshwater green alga, *Selenastrum capricornutum*, under static conditions, over a period of 96 hours. The measured endpoints were cell density, area under the growth curve, and growth rate. Three replicate growth chambers were used for each treatment group and for the negative control group. Nominal test concentrations were 63, 130, 250, 500 and 1000 ug/l. The actual water concentrations were measured at 0 and 96 hours. At test initiation, each chamber received an inoculum of 10,000 alga cells/ml. During the test, samples were collected from each chamber at approximately 24 hour intervals to determine cell densities, which were used to calculate areas under the curve (biomass) and growth rates. These values were used to determine percent inhibition values. The algal cultures, if not inhibited, should show exponential growth over the 96-hour exposure period. Water temperature, pH, and light intensity were measured. EC50 values were calculated.

Results: The growth chambers were maintained at 24°C. The pH was 7.9 on day 0 and 9.6 at 96 hours. Light intensity ranging from 3910 to 4710 lux. The actual measured growth chamber concentrations were 52, 112, 233, 485, and 1011 ug/l, representing 82, 86, 93, 98, and 101% of the nominal test substance concentrations. The 72 and 96 hour EC50, based on cell density, area under the curve, and growth rate, was >1011 ug/l, the highest concentration tested. The 96 hour NOAEC, based on cell density, was 112 ug/l.

Conclusion: The NOAEC for is 112 ug/l, and the EC50 is greater than 1011 ug/l.
Reliability: 1
Reference: 11

5. Mammalian Toxicity

5.1 Acute Toxicity

5.11 Acute Oral Toxicity

Identity: Phosflex TXP (Lot No. E-94163)
Guideline: OECD Guideline 401 Acute Oral Toxicity
Year: 1995
GLP: Yes
Species: Rat
Strain: Sprague-Dawley
Method: Five male and 5 female rats were fasted for 24 hours after which they received a single 20,000 mg/kg oral gavage dose of trixylenyl phosphate. The animals were observed daily for 14 days for signs of toxicity and for mortality. Body weights were determined on study days 0, 7, and 14. The animals were then sacrificed and necropsied. At necropsy, internal structures and organs were visually examined for gross lesions.
Results: There was no mortality. Signs of toxicity included lacrimation and staining of the fur around the nose. There was a slight depression of body weight during the first week, but body weights increased during the second week. No gross abnormalities were observed at necropsy. The acute oral LD50 is greater than 20,000 mg/kg.
Conclusion: Trixylenyl phosphate demonstrated very low acute oral toxicity. The acute oral LD50 is greater than 20,000 mg/kg.
Reliability: 1
Reference: 12

Identity: Fyrquel EHC (Lot No. 9221-J-1-1X)
Guideline: EPA OTS 798.1175 Acute Oral Toxicity
Year: 1984
GLP: Yes
Species: Rat
Strain: Sprague-Dawley
Method: Ten male and 10 female rats were fasted for 24 hours after which they received a single 5,000 mg/kg oral gavage dose of trixylenyl phosphate. The animals were observed daily for 14 days for signs of toxicity and for mortality. Body weights were determined on study days 0, 7, and 14. The animals were then sacrificed and necropsied. At necropsy, internal structures and organs were visually examined for gross lesions.
Results: No animals died during this 14 day study. Signs of toxicity included mild depression, piloerection, wet fur, diarrhea, and stained fur. All symptoms disappeared by study day 7. Gross examination of the internal organs at necropsy found no treatment-related changes. The acute oral LD50 is greater than 5000 mg/kg.

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Conclusion: Trixylenyl phosphate demonstrated low acute oral toxicity. The oral LD50 was determined to be greater than 5000 mg/kg.
Reliability: 1
Reference: 13

5.12 Acute Dermal Toxicity

Identity: Fyrquel EHC (Lot No. 9221-J-1-1X)
Guideline: EPA OTS 798.1100
Year: 1984
GLP: Yes
Species: Rabbit
Strain: New Zealand White
Method: Abdominal fur on 5 male and 5 female New Zealand White rabbits was closely clipped and the skin was abraded on half the animals. The skin on the other half of the animals was left intact. Twenty-four hours later, trixylenyl phosphate was applied neat at 2000 mg/kg to the clipped area, which was then wrapped with a gauze binder. After 24 hours the gauze binder was removed. The animals were observed daily for 14 days following treatment for signs of toxicity. Necropsies were conducted on day 15 on all animals. Internal organs were examined for gross lesions.
Results: There were no deaths during the 14 day observation period. Mild erythema and edema was observed 24 hours after the application of the test substance to the skin, but these skin effects disappeared by 48 hours. There were no clinical signs other than the mild erythema and edema. There were no treatment-related lesions observed during necropsy. The acute dermal LD50 is greater than 2000 mg/kg.
Conclusion: Trixylenyl phosphate demonstrated low acute dermal toxicity. The acute dermal LD50 is greater than 2000 mg/kg.
Reliability: 1
Reference: 14

5.13 Skin Irritation

Identity: Fyrquel EHC (Lot No. 9221-J-1-1X)
Guideline: EPA OTS 798.4470
Year: 1984
GLP: Yes
Species: Rabbit
Strain: New Zealand White
Method: An area of skin on the backs of six rabbits was shaved and half the shaved areas were abraded 24 hours prior to dosing. Each animal received 0.5 ml of trixylenyl phosphate on the shaved area. The application sites were then immediately wrapped with a gauze dressing for

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4 hours, then unwrapped at which time the remaining test substance was removed. The animals were observed for signs of skin irritation at 4, 24, 48, and 72 hours after the application of trixylenyl phosphate. The degree of irritation was rated using the Draize scoring method at each observation.

Results: All six rabbits showed mild erythema through 24 hours after treatment at both the abraided and nonabraided application sites. No edema was observed. At 72 hours, two animals continued to show very mild erythema. The Primary Irritation Score was 0.70 indicating that trixylenyl phosphate is a mild dermal irritant.

Conclusion: Trixylenyl phosphate is a mild skin irritant.

Reliability: 1

Reference: 15

5.14 Eye Irritation

Identity: Fyrquel EHC (Lot No. 9221-J-1-1X)

Guideline: EPA OTS 798.4500

Year: 1984

GLP: Yes

Species: Rabbit

Strain: New Zealand White

Method: A dose of 0.1 ml of trixylenyl phosphate was placed in the everted lower left eyelid of 9 rabbits. The upper and lower lids were then held together for about one second. About 30 seconds after treatment, the treated eyes of 3 rabbits were gently flushed with water for about 1 minute. The treated eyes of the remaining 6 rabbits remained unwashed. The right eye of each rabbit served as an untreated control eye. Each treated eye was scored for irritation at 1, 24, 48, and 72 hours and at 4 and 7 days after treatment. Fluorescein was used during the 24 hour eye examinations. The eyes were scored for irritation using the Draize method and rating scale.

Results: Mild to moderate irritation was observed at 1 hour in both washed and unwashed treated eyes of all 9 animals. It consisted of redness of the conjunctiva. There were no effects on the cornea or iris. The irritation was gone by at the 24 hour observation. Trixylenyl phosphate is a mild eye irritant.

Conclusion: Trixylenyl phosphate is a mild eye irritant.

Reliability: 1

Reference: 16

5.2 Combined Repeated Dose and Reproductive/Developmental Toxicity Screening Study

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|------------|--|
| Identity: | Phosflex TXP (Lot # 02223D0200 T#127) |
| Guideline: | OECD 422 |
| Year: | 2004 |
| GLP: | Yes |
| Species: | Rat |
| Strain: | Sprague-Dawley |
| Route: | Oral gavage |
| Method: | <p>Trixylenyl phosphate was administered daily by oral gavage, 7 days per week, to 11 male and 11 female rats per group at doses of 0, 25, 200, or 1000 mg/kg for two weeks prior to mating, during mating, through gestation, and through lactation. An additional 5 animals per sex were included in the high dose and control groups as recovery animals, and were held for 4 weeks after dosing stopped. The recovery animals were mated at the end of the 4 week recovery period, their blood parameters were measured, and the tissues from these recovery animals were examined via diagnostic pathology. Parameters measured in this study include body weights, food consumption, hematology, clinical chemistry, successful matings, fertility, number of pregnancies, litter size, and histopathology of the reproductive organs and the major organs. Functional observational batteries and motor activity measurements were conducted to measure for neurotoxic activity.</p> |
| Results: | <p>Food consumption and body weight gain were slightly reduced in the 1000 mg/kg/day group after the first week of treatment. During the later part of gestation, dam food consumption, body weight, and body weight gain were lower in the 200 and 1000 mg/kg/day groups. This was attributed to the lower rate of successful pregnancies in those groups. Clinical chemistry profiles showed changes in certain serum chemistry parameters, including elevated blood urea nitrogen and ALT in one or both sexes of the 200 and 1000 mg/kg/day groups, while plasma cholinesterase activity was reduced in both sexes in the mid and high dose animals. Gross necropsy findings were insignificant. Organ weight data indicated that the adrenals, testes, epididymides, ovaries, heart, and liver were target organs. With the exception of the heart, morphological alterations were observed in each of these organs. There were no differences in functional observation battery and motor activity measurements between the treated animals and the untreated control group, indicating a lack of neurotoxic activity.</p> <p>The number of successful matings was the same in each group, as determined by the number of sperm positive females, indicating that treatment with trixylenyl phosphate does not adversely affect mating performance. However, the reproductive outcome from the successful matings was adversely affected in the mid- and high dose animals. Full</p> |

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term (successful) pregnancies occurred in 100 % of the control and low dose animals, 18% in the mid dose, and 0% in the high dose groups. The mating of the male and female high dose recovery animals resulted in 100% successful pregnancies, indicating that the adverse reproductive effect is fully reversible in 4 weeks after cessation of treatment. Whether the reproductive effect occurs in the male or female animals, or in both sexes, is not known. Microscopic examination of the reproductive organs found treatment-related degenerative changes in the testes and ovaries, suggesting that both sexes are adversely affected. Although pregnancy and delivery of litters in the low dose animals were unaffected by treatment, there were slight degenerative changes in the male and female reproductive organs in the animals of this group, indicating a lack of an NOAEL in this study.

Conclusion: Daily exposure to trixylenyl phosphate for several weeks resulted in a decrease in pregnancies, indicating the test substance is a reproductive toxin. It was also shown that the infertility fully reverses within 4 weeks after the exposure is discontinued.

Reliability: 1

Reverence: 17

5.3 Genetic Toxicity

5.3.1 In Vitro Gene Mutation

Identity: Phosflex TXP (Lot No. T#127)
Guideline: OPPTS 870.5100 and OECD 471
Test Type: Bacterial Reverse Mutation Test (Ames Test)
Year: 2003
GLP: Yes
Method: Five tester strains of *Salmonella typhimurium*, TA-1535, TA-1537, TA-1538, TA-98, and TA-100, and one strain of *Escherichia coli*, WP2 uvrA, were exposed to trixylenyl phosphate in the presence and absence of a metabolic activating system to determine whether the test substance can induce base-pair and/or frame-shift mutations. Doses used were 33.3, 100, 333, 1000, 3330, and 5000 ug per plate. Positive control chemicals were included in the assay, as were solvent (DMSO) and negative control groups. To meet EU/OECD requirements, confirmatory assays were conducted.

Results: The positive control chemicals significantly increased the number of revertants per plate, confirming that the assay was sensitive to, and responsive to, mutagenic chemicals. Trixylenyl phosphate did not increase the number of revertants per plate and thus did not cause mutation in the test system, either in the presence or absence of a metabolic activating system.

Conclusion: Trixylenyl phosphate did not express mutagenic activity in this test.

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Reliability: 1
Reference: 18

Identity: Trixylenyl Phosphate
Guideline: EPA OTS 798.5265
Test Type: Bacterial Reverse Mutation Test (Ames Test)
Year: 1984
GLP: Yes
Method: Trixylenyl phosphate was tested for gene mutation in four tester strains, TA-1535, TA-1537, TA-98, and TA-100, in the presence and absence of an induced rat liver metabolic activating system. Negative control, solvent control (DMSO), and positive control groups were included in the test. Doses used in this test were 2, 6, 18, 54, and 162 ug per plate.

Results: Trixylenyl phosphate did not induce mutations in any of the four tester strains, either in the presence or absence of a metabolic activating system. The positive control chemicals induced a significant increase in mutations, confirming the sensitivity of the assay.

Conclusion: Trixylenyl phosphate did not demonstrate mutagenic activity in this assay.
Reliability: 4
Reference: 19

5.3.2 In Vitro Chromosome Aberrations

Identity: Phosflex TXP (Lot No. T#127)
Guideline: OPPTS 870.5375
Test Type: Chromosomal Aberrations in Chinese Hamster Ovary Cells
Year: 2003
GLP: Yes
Method: Chinese hamster ovary cells were exposed to several concentrations of trixylenyl phosphate, in the presence and absence of a metabolic activating system. The doses used in this assay were 3.38, 4.84, 6.92, 9.89, 14.1, 20.2, 28.8, 41.2, 58.8, 84.0, 120, 172, 245, 350, and 500 ug/ml. Negative control, solvent control (DMSO), and positive control groups were included in the study. After incubating the cells with trixylenyl phosphate, the cells were examined for chromosomal aberrations, including chromosomal breaks, chromatid exchanges, and rearrangements. A confirmatory assay was conducted to meet EU/OECD requirements.

Results: Trixylenyl phosphate did not induce chromosomal aberrations in the Chinese hamster ovary cells in the presence or absence of metabolic activation. The positive control chemicals caused a significant increase in aberrations, confirming the sensitivity of the assay. Trixylenyl phosphate did not demonstrate mutagenic activity in this test.

Conclusion: Trixylenyl phosphate did not demonstrate mutagenic activity.
Reliability: 1
Reference: 20

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5.4 Neurotoxicity

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|--------------|--|
| Identity: | Fyrquel EHC (Lot No. 4795-13-6) |
| Guideline: | EPA OTS Guideline for Acute Neurotoxicity Testing – 1978 |
| Test Type: | Acute Delayed Neurotoxicity Test |
| Year: | 1980 |
| GLP: | No |
| Species: | Hen |
| Strain: | White Leghorn |
| Method: | Seven adult White Leghorn hens received a 11.4 g/kg dose of trixylenyl phosphate by oral gavage. An additional 4 hens received corn oil as the negative control group. Four other hens received 250 mg/kg TOCP as the positive control group. Three of the trixylenyl phosphate treated hens were observed daily for three weeks for behavioral changes and changes in gait. The remaining 4 hens that received test substance were sacrificed about 24 hours after dosing, at which time their brains were removed and processed for enzyme analysis. Neurotoxic esterase (NTE) and cholinesterase activity were measured in the brains of the trixylenyl phosphate treated hens, and also in the brains of the TOCP treated hens and the negative control hens. |
| Results: | The 3 hens that were observed for behavioral and gait changes after receiving 11.4 g/kg trixylenyl phosphate showed no adverse effects for 9 days, after which motor incoordination became apparent. The severity of the incoordination increased up to the time the hens were sacrificed. The degree of ataxia observed was similar in intensity to that normally seen after TOCP treatment. In the 4 hens sacrificed 24 hours after dosing, trixylenyl phosphate treatment resulted in brain cholinesterase inhibition of about 85% and brain NTE inhibition of about 94%. TOCP, the positive control neurotoxin, inhibited brain cholinesterase and NTE activity by about 73% and 89% respectively. The test substance demonstrated a degree of neurotoxic activity similar to that observed for the positive control chemical. |
| Conclusion: | Trixylenyl phosphate demonstrated substantial neurotoxic activity. |
| Reliability: | 1 |
| Reference: | 21 |
| Identity: | Fyrquel EHC (Lot No. 4795-13-6) |
| Guideline: | EPA OTS Guideline for Acute Neurotoxicity Testing – 1978 |
| Test Type: | Acute Delayed Neurotoxicity Test |
| Year: | 1981 |
| GLP: | Yes |
| Species: | Hen |
| Strain: | White Leghorn |
| Method: | Trixylenyl phosphate was administered as a single dose by oral gavage to groups consisting of 4 adult White Leghorn hens each, at dose levels of 11.4, 114, or 1140 mg/kg. A negative control (corn oil) group consisting |

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of 4 hens and a positive control group (TOCP) containing 8 hens were included in the study. The endpoints measured were brain cholinesterase activity and brain neurotoxic esterase (NTE) activity. About 24 hours after treatment, the animals were sacrificed and their brains immediately removed for processing for enzyme activity measurements. This study utilized three doses to determine if there was a dose-response with the enzyme inhibition, and whether an NOAEL could be established.

Results: Percent NTE inhibition for the low, mid, and high dose groups were 2.0, 13.4, and 55.8%, respectively. The positive control chemical inhibited NTE by 90.3%. Since an inhibition of NTE of greater than 70% is thought to be necessary to elicit neurotoxic activity, all three trixylenyl phosphate doses should not induce neurotoxicity (neuropathy). Cholinesterase inhibition was inhibited in the mid and high dose animals, and in the positive control animals. The dose-response observed for neurotoxicity suggests a significant margin of safety exists for individuals accidentally exposed to small amounts of trixylenyl phosphate.

Conclusion: Trixylenyl phosphate did not demonstrate the level of NTE inhibition associated with the induction of neurotoxicity.

Reliability: 1

Reference: 22

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References

1. Sax, N. and Lewis, R., Eds. Hawley's Condensed Chemical Dictionary. 11th Edition, New York, Van Nostrand Reinhold Company, 1987. Page 1179
2. Hazardous Substance Data Bank, National Library of Medicine, 2004,
3. Wildlife International Ltd., Final Report for Project No. 497C-156. Determination of Water Solubility of Phosflex TXP. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
4. Saeger, v.w., Hicks, O., Kaley, R.G., and Tucker, E.S. Environmental fate of selected phosphate esters. Environ. Sci. Technol. 13:840-844. 1979.
5. Wildlife International Ltd., Final Report for Project No. 497C-155. Determination of the Ultraviolet-Visible Absorption Spectrum of Phosflex TXP. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
6. Wildlife International Ltd., Final Report for Project No. 497C-154. Phosflex TXP: An Evaluation of Hydrolysis as a Function of pH. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
7. Wildlife International Ltd., Final Report for Project No. 497E-104. Phosflex TXP: Closed Bottle Test for Ready Biodegradability. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
8. Wildlife International Ltd., Final Report for Project No. 497A-127. Phosflex TXP: A 96 Hour Flow-Through Acute Toxicity Test with the Fathead Minnow. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
9. Union Carbide Environmental Services Laboratory, Final Report for Project No. 11506-92-10. The Acute Toxicity of Fyrquel EHC to the Rainbow Trout. Study conducted for Stauffer Chemical Company, 1979.
10. Wildlife International Ltd., Final Report for Project No. 497A-126C. Phosflex TXP: A 48-Hour Static-Renewal Acute Toxicity Test with the Cladoceran, *Daphnia magna*. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
11. Wildlife International Ltd., Final Report for Project No. 497A-128. Phosflex TXP: A 96-Hour Toxicity Test with the Freshwater Alga *Selenastrum capricornutum*. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
12. Hazelton Wisconsin, Inc. Study No. HWI 41001596. Acute Oral Toxicity Study of E-94163 in Rats. Conducted for Akzo Nobel Chemicals Inc. , 1995.
13. Stauffer Chemical Company study No. T-10962. Acute Oral Toxicity Study in Rats. 1984.
14. Stauffer Chemical Company study No. T-10962. Acute Dermal Toxicity Study in Rabbits. 1984.
15. Stauffer Chemical Company study No. T-10962. Primary Skin Irritation Study in Rabbits. 1984.
16. Stauffer Chemical Company study No. T-10962. Primary Eye Irritation Study in Rabbits. 1984.
17. Experimur study No. 03-246. Combined Oral Repeated Dose and Reproductive/ Developmental Toxicity Screening Test of Phosflex TXP in Rats. Study conducted for Akzo Nobel Functional Chemicals LLC, 2004.
18. Covance Laboratories Inc. Final Report for Study No. 6950-116. *Salmonella-Escherichia coli*/Mammalian Microsome Reverse Mutation Assay with a Confirmatory Assay with

Trixylenyl Phosphate – Robust Summaries

- Phosflex TXP. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
19. Ciba-Geigy Ltd. Study. Salmonells/Mammalian Microsome Mutagenicity Test with TK 10 509 (Reofos 95). Study conducted in 1984. Information on this test obtained from a Toxline search, referenced as EPA/OTS Doc. #40-8442159.
 20. Covance Laboratories Inc. Final Report for Study No. 24695-0-437OECD. Chromosomal Aberrations in Chinese Hamster Ovary (CHO) Cells with Phosflex TXP. Study conducted for Akzo Nobel Functional Chemicals LLC, 2003.
 21. Stauffer Chemical Company Study No. T-10264. Neurotoxicity Evaluation of Fyrquel EHC. 1980.
 22. Stauffer Chemical Company Study No. T-10552. Effect of Three Doses of Fyrquel EHC on Neurotoxic Esterase. 1981.